REMARKS / ARGUMENTS

Claims 12-30 are pending. Claims 22-30 are withdrawn and claims 1-11 are canceled consistent with the election of claims previously entered. Claims 17-21 are amended. Support for these amendments may be found in the original claims and in the specification at page 6, lines 7-19.

Specification Objections

> The Examiner has objected to the abstract of the disclosure as allegedly lacking sufficient description of the elected invention. Further, the Examiner has required amendment of references to the trademark CREMOPHOR EL within the specification.

Without addressing the merits of the Examiner's requirement, Applicants have amended the Abstract of the Disclosure to further detail the parenteral formulations, and processes for preparation thereof, which are claimed herein. In addition, references to CREMOPHOR® EL in the specification have been amended as requested to reflect the status of this term as a registered trademark by BASF. CREMOPHOR® EL is the brand name for a polyethoxylated castor oil, which is a mixture of ricinoleic acid, polyglycol ester, glyerol polyglycol esters, and polyglycols. The polyethoxylated castor oil is also known under the common names polyethyleneglycerol triricinoleat 35 (DAC) or polyoxyl 35 castor oil.

In view of these amendments, the Examiner is respectfully requested to reconsider and withdraw these objections.

Claims Objections

> The Examiner has objected to claims 17-21 as allegedly technically or grammatically incorrect.

Without addressing the merits of the Examiner's objections, Applicants have amended claims 17-21 consistent with the recommendation of the Examiner. In view of these amendments, the Examiner is respectfully requested to reconsider and withdraw these objections.

Claims Rejections - 35 USC §102

> The Examiner has rejected claims 12, 13, and 15 under 35 USC §102(e) and (a) allegedly anticipated by US Patent Publication No. US 2002/0013335 ("Azrolan").

Applicants respectfully disagree that Azrolan anticipates any of claims 12, 13, or 15. Claim 12 provides a parenteral formulation comprising CCI-779, an alcoholic solvent, an antioxidant, a diluent solvent, and a surfactant. A formulation having these components is not described in Azrolan.

At paragraph 0028 of Azrolan, "solutions or suspensions" are described having an active compound and water mixed with a surfactant. Dispersions "*can also be prepared*" (emphasis added) according to Azrolan prepared in "glycerol, liquid polyethylene glycol, and mixtures thereof in oils." Claim 14 provides a method of treatment comprising administering a rapamycin and an antioxidant.

There is no single parenteral formulation described in Azrolan which comprises CCI-779, an alcoholic solvent, an antioxidant, a diluent solvent, and a surfactant. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this ground of rejection.

Claims Rejections - 35 USC §103

> The Examiner has rejected claims 12-21 under 35 USC §103(a) as allegedly unpatentable over Azrolan in view of US Patent No. 5,516,770 ("Waranis") and United Kingdom Patent Application No. GB 237611 ("Haeberlin").

Applicants respectfully disagree that this combination of documents renders the claims obvious. As indicated above, claim 12 provides a parenteral formulation comprising CCI-779, an alcoholic solvent, an antioxidant, a diluent solvent, and a surfactant. A formulation having these components is not suggested by these documents.

As discussed above, Azrolan does not describe a single parenteral formulation which comprises CCI-779, an alcoholic solvent, an antioxidant, a diluent solvent, and a surfactant. Waranis and Haeberlin add nothing to Azrolan that would lead one of skill in the art to the present formulations. Waranis describes solutions of rapamycin

in propylene glycol to be mixed with a water diluent solution containing polyethylene glycol 200, 300, and/or 400, and a polyoxyethylene sorbitan ester in injectable form. No antioxidant is described. Haeberlin describes the stabilization of rapamycins and ascomycins (*e.g.*, FK-506) by formulation in acid, including malonic acid, oxalic acid, citric acid, and lactic acid. However, it does not recognize the benefit of antioxidants over acids generally in stabilizing macrolides.

In combination, one of skill in the art is not lead to solving the problems of preparing CCI-779 parenteral formulations, *i.e.*, chemical stability and precipitation upon dilution, nor do they provide any motivation to solve these problems. Absent recognition of the problems addressed by the claimed formulations, one of skill in the art could not arrive at the claimed formulations absent hindsight in view of the advantages identified by the Applicants.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw this ground of rejection.

In view of the amendments presented and the above remarks, the Examiner is respectfully requested to reconsider and withdraw all pending objections and rejections and permit the application to pass to issue.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper, or credit any overpayment in any fees, to our Deposit Account, Number 08-3040.

Respectfully submitted,

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